

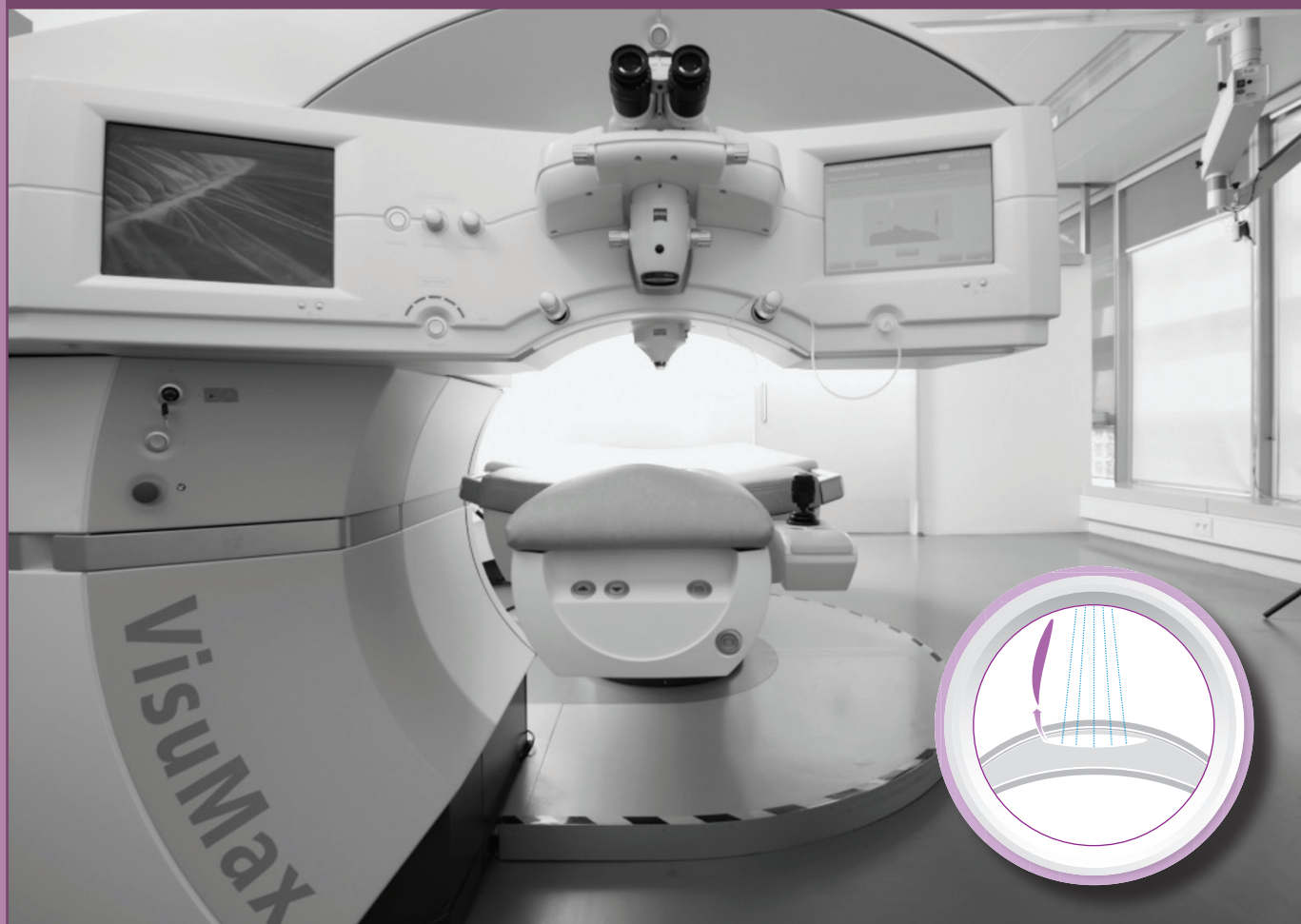
# Cataract & Refractive Surgery

**EUROPE**

**TODAY**

## UPDATE ON SMILE

Latest findings on the 3<sup>rd</sup> generation of laser vision correction.



**LASER VISION CORRECTION BEYOND PRK AND LASIK**

# Current Status of SMILE

This intrastromal form of keratomileusis is the 3<sup>rd</sup> generation in refractive surgery techniques.

BY DAN Z. REINSTEIN, MD, MA(CANTAB), FRCSC, DABO, FRCOPHTH, FEBO

Ever since femtosecond lasers were introduced into refractive surgery, the ultimate goal has been to create an intrastromal lenticule that can be removed manually in one piece, thereby circumventing the need for incremental photoablation by an excimer laser. Early studies with picosecond<sup>1</sup> and femtosecond lasers<sup>2</sup> did not culminate in actual clinical trials; however, following the introduction of the VisuMax femtosecond laser (Carl Zeiss Meditec) in 2007,<sup>3</sup> the intrastromal lenticule method was reintroduced in a procedure called *femtosecond lenticule extraction* (ReLEx FLEX). This procedure involved lifting a flap to allow the removal of the lenticule.<sup>4-6</sup>

Given the success of ReLEx FLEX, the procedure evolved into its current small-incision, flapless form, which is known as *ReLEx SMILE*. This technique involves creating one or two small incisions (Figure 1) through which the lenticule interfaces can be separated, allowing the lenticule to be removed without creating a flap. The results of the first prospective trials of SMILE have been published,<sup>7-9</sup> and subsequent studies have shown the visual and refractive outcomes to be similar to LASIK.<sup>10-15</sup>

The VisuMax is currently the only commercially available femtosecond laser being used for intrastromal lenticular surgery (SMILE). In order for accurate three-dimensional (3-D) intrastromal cutting to be achieved, Carl Zeiss Meditec had to overcome several technological hurdles. Namely, not only does the accuracy of femtosecond 3-D pulse placement need to be high and the pulse energy low, but tissue distortion in the cornea must be minimized when optically coupling to the femtosecond laser source.

## DESIGN ELEMENTS

Six distinct design elements of the VisuMax represent how the device achieves high-precision intracorneal lenticular cutting.

**Element No. 1.** The coupling contact glass is curved in order to minimize corneal distortion.

**Element No. 2.** The coupling suction

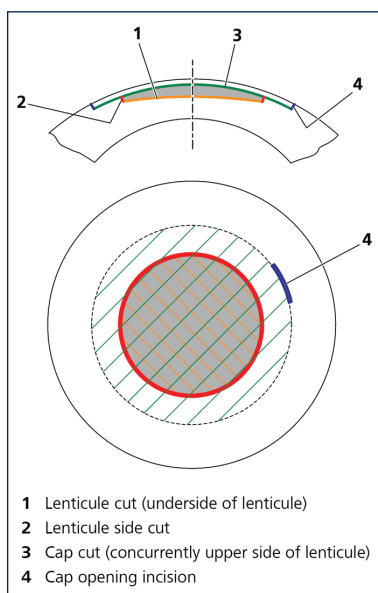
is applied to the peripheral cornea, not the conjunctiva and sclera. This further minimizes corneal distortion and allows immobilization of the cornea using a low suction force.

**Element No. 3.** Each treatment is individually calibrated based on the detection of individual tolerances of the contact glass, when attached to the laser device.

**Element No. 4.** The optical beam path is suspended on a fulcrum with force-feedback servo control of the height of the patient bed and headrest, thus maintaining a consistent force onto the cornea.

**Element No. 5.** The beam's high numerical aperture is designed to deliver tight concentration of femtosecond laser energy with low per-pulse energy load.

**Element No. 6.** The high pulse repetition rate (500 kHz) minimizes treatment time.



**Figure 1. Incision geometry of the SMILE procedure.** The lenticule cut is performed on the underside of the lenticule (1), followed by the lenticule sidecuts (2). The cap interface is created on the upper side of the lenticule (3), and finally a 2- to 3-mm small incision is created super-temporally (4). The lenticule interfaces are separated using a flap separator and the lenticule is extracted manually, all via the small incision.

## ADVANTAGES OF SMILE

When compared with LASIK and PRK treatments, SMILE has three distinct advantages.

### Advantage No 1: More accurate and repeatable tissue removal.

Intrastromal lenticule procedures may have advantages over LASIK and PRK because the potential errors associated with excimer laser ablation such as stromal dehydration,<sup>16</sup> laser fluence projection and reflection losses,<sup>17</sup> and other environmental factors<sup>18</sup> are avoided. Also, the cutting time in SMILE is always the same, and it is independent from the refraction. Tissue removal is defined only by the accuracy of the femtosecond laser, a device that is not affected by any changes in environmental conditions. This accuracy is demonstrated by the 4.4-μm reproducibility of cap thickness<sup>19-21</sup> and, as a result, it is likely that there will be less need for personalized nomograms for different machines, locations, or surgeons.

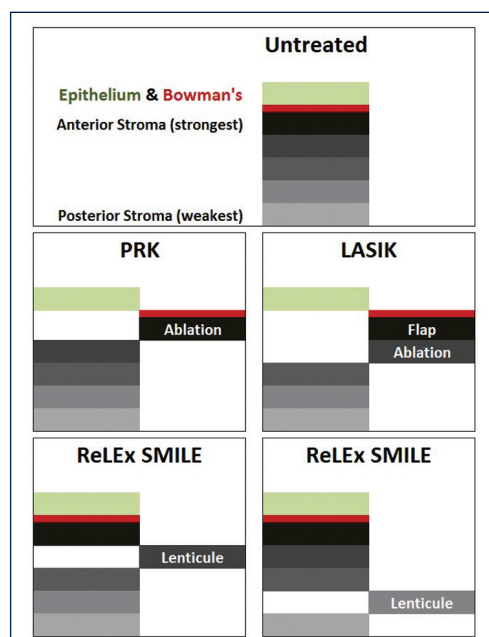
**Advantage No 2: Increased biomechanical integrity.** Two characteristics of the SMILE treatment, the absence of a flap and stromal tissue removal from within the stroma, mean that

the anterior-most stromal lamellae remain intact postoperatively, except for in the region of the small incision. In comparison, the anterior stromal lamellae are severed during LASIK by the creation of the flap and the excimer laser ablation, and by the excimer laser ablation during PRK. Because the anterior corneal stroma is the strongest part of the stroma,<sup>22</sup> SMILE leaves the cornea with greater biomechanical strength than LASIK and PRK.

Randleman et al<sup>22</sup> measured the tensile strength of strips of stromal lamellae cut from different depths within the cornea and found a strong negative correlation between stromal depth and tensile strength. The anterior 40% of the central corneal stroma was the strongest region of the cornea, whereas the posterior 60% was at least 50% weaker. Similar results for the nonlinear nature of stromal tensile strength have been reported by Scarcelli et al<sup>23</sup> using Brillouin microscopy.

Surgeons are accustomed to calculating the residual stromal thickness in LASIK as the amount of stromal tissue left under the flap, and therefore the first instinct is to apply this rule to SMILE. However, the actual residual stromal thickness in this procedure should be calculated as the total uncut stroma (ie, the stroma above and below the lenticule; Figure 2). Given the decreasing strength of stroma with depth, a more crucial factor than residual stromal thickness is tensile strength. In order to consider this factor, we have developed a postoperative tensile strength calculator<sup>24</sup> based on Randleman's data.<sup>22</sup> Our model predicted that the postoperative tensile strength after SMILE was approximately 10% higher than PRK and 25% higher than LASIK.

We can take advantage of this difference in postoperative biomechanics to improve the optical quality of the outcome by better controlling the induction of spherical aberration. Our studies have shown that the same spherical aberration is induced for the spherical SMILE lenticule profile in a 6-mm zone as is by the aspherically optimized Laser Blended Vision ablation profile, but with less tissue removal with the SMILE profile.<sup>25</sup> Therefore, spherical aberration control can be improved in SMILE by increasing the optical zone, even if this means greater tissue removal, as the postoperative tensile strength is still much higher postoperatively. For example, in an eye with central pachymetry of 588  $\mu\text{m}$ , a 7-mm zone was used to treat -10.00 D (203  $\mu\text{m}$



**Figure 2.** The differences in strength of the remaining stroma after PRK, LASIK, and SMILE. These diagrams demonstrate that the strength of the stroma remaining after SMILE is greater than the equivalent treatments in PRK and LASIK. Because the Bowman layer remains intact with SMILE, there is added strength. Also, the two diagrams for SMILE demonstrate the even greater strength if the lenticule is removed from deeper within the stroma.

tissue removal) with a 135- $\mu\text{m}$  cap thickness. The stromal thickness under the lenticule was 250  $\mu\text{m}$ , but the total uncut stromal thickness was 335  $\mu\text{m}$ , which represents a postoperative tensile strength of 58%. In comparison, a -10.00 D LASIK treatment in which a 6-mm optical zone was used with a 100- $\mu\text{m}$  flap left a residual stromal thickness of 298  $\mu\text{m}$ , representing a postoperative tensile strength of 44%. The spherical aberration induced was only 0.15  $\mu\text{m}$  in the SMILE case and 0.75  $\mu\text{m}$  in the LASIK case (Figure 3).

This example demonstrates how we can safely use SMILE to achieve an acceptable postoperative tensile strength. For this eye with pachymetry of 588  $\mu\text{m}$ , we would be able to treat -16.00 D in a 7-mm zone, leaving 250  $\mu\text{m}$  of total uncut stroma (but only 168  $\mu\text{m}$  under the lenticule), and a postoperative tensile strength of 44%. The predicted spherical aberration induction for this correction would be only 0.39  $\mu\text{m}$ , which is still better than the -10.00 D LASIK.

Finally, there is also the possibility of treating thinner corneas with SMILE. For example, the same -10.00 D correction in a 7-mm zone could be done in a 490  $\mu\text{m}$  cornea, leaving 236  $\mu\text{m}$  total uncut stroma (154  $\mu\text{m}$  under the lenticule) and still have a postoperative tensile strength of 53%.

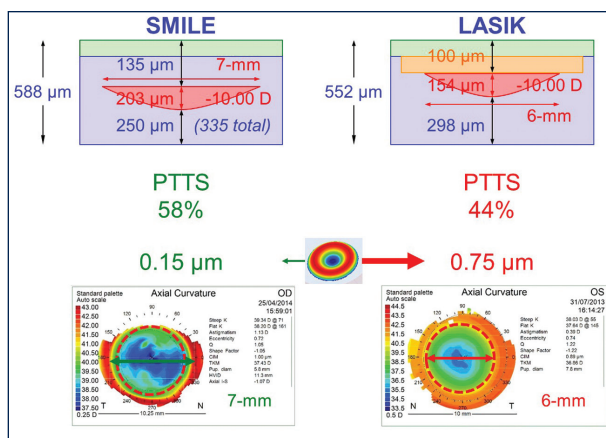
In summary, the superior tensile strength provided by preserving the stronger anterior stroma in SMILE allows larger optical zones, thus improving spherical aberration control and, hence, optical quality. This is achieved while leaving the cornea stronger than LASIK leaves the stroma.

#### **Advantage No 3: Reduction in postoperative dry eye.**

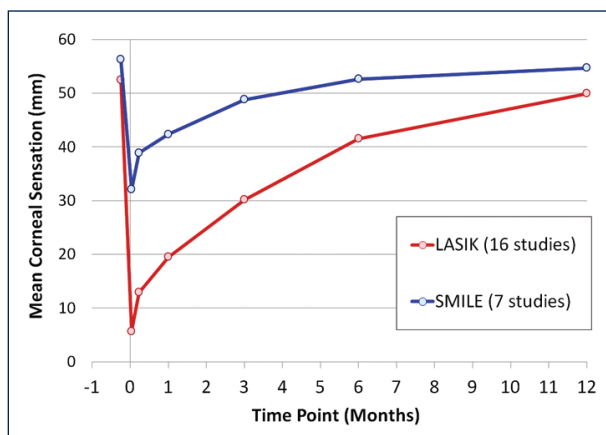
The cornea is one of the most densely innervated peripheral tissues in humans, with the majority of the nerve bundles within the anterior stroma. These anterior nerves are cut by the microkeratome or femtosecond laser in LASIK and by the ablation in PRK, which results in dry eye symptoms.

On the other hand, the anterior stromal nerve plexus is disrupted significantly less with SMILE since no sidecut is created and the lenticule position is in deeper corneal layers. This should result in fewer dry eye symptoms and faster recovery of patient comfort postoperatively. Indeed, several studies have shown the faster recovery of corneal sensation after SMILE,<sup>26-33</sup> with recovery to baseline by 3 months compared with 6 to 12 months after LASIK. Figure 4 shows the average corneal sensation from the SMILE studies compared





**Figure 3.** Line graph showing the mean central corneal sensation over 12-month follow-up averaged across seven SMILE studies and 16 LASIK studies following a review of the peer-reviewed literature.



**Figure 4.** The average corneal sensation from the author's SMILE study compared with 16 LASIK studies.

with 16 LASIK studies where the same Cochet-Bonnet aesthesiometry technique was used. (For more information on corneal sensation, please see Preserving Corneal Neural Architecture on page 14.)

## CONCLUSION

With the introduction of the VisuMax femtosecond laser technology, it has become clinically feasible to create refractive lenticules of proper regularity with sufficient accuracy to meet—and probably exceed—the accuracy of excimer laser tissue ablation for corneal refractive corrections. This allows surgeons to achieve Jose Ignacio Barraquer's original concept of keratomileusis through a minimally invasive pocket incision, with maximal retention of anterior corneal innervation and structural integrity. It is the next frontier in perfect refractive surgical techniques for patients and surgeons alike. ■

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of Ophthalmology, Columbia University Medical College, New York, and the Centre Hospitalier National d'Ophtalmologie, Paris. Dr. Reinstein states that he is a consultant to Carl Zeiss Meditec and has a proprietary interest in the Artemis technology (ArcScan) and is an author of patents related to VHF digital ultrasound administered by the Cornell Center for Technology Enterprise and Commercialization. He may be reached at tel: +44 207 224 1005; fax +44 207 224 1055; e-mail: dzz@londonvisionclinic.com.

1. Ito M, Quattrone AJ, Malhan S, et al. Picosecond laser in situ keratomileusis with a 1053-nm Nd:YLF laser. *J Refract Surg.* 1996;12:721-728.
2. Kurtz RM, Horvath C, Liu HH, et al. Lamellar refractive surgery with scanned intrastromal picosecond and femtosecond laser pulses in animal eyes. *J Refract Surg.* 1998;14:541-548.
3. Reinstein DZ, Archer TJ, Gobbe M, et al. Accuracy and reproducibility of Artemis central flap thickness and visual outcomes of LASIK with the Carl Zeiss Meditec VisuMax Femtosecond Laser and MEL 80 Excimer Laser Platforms. *J Refract Surg.* 2010;26:107-119.
4. Sekundo W, Kunert K, Russmann C, et al. First efficacy and safety study of femtosecond lenticule extraction for the correction of myopia: six-month results. *J Cataract Refract Surg.* 2008;34:1513-1520.
5. Blum M, Kunert KS, Engelbrecht C, et al. Femtosecond lenticule extraction (FLEx) - Results after 12 months in myopic astigmatism. *Klin Monbl Augenheilkd.* 2010;227:961-965.
6. Vestergaard A, Ivarsen A, Asp S, et al. Femtosecond (FS) laser vision correction procedure for moderate to high myopia: a prospective study of RelEx flex and comparison with a retrospective study of FS-laser in situ keratomileusis. *Acta Ophthalmol.* 2013;91(4):355-362.
7. Sekundo W, Kunert KS, Blum M. Small incision corneal refractive surgery using the small incision lenticule extraction (smile) procedure for the correction of myopia and myopic astigmatism: results of a 6 month prospective study. *Br J Ophthalmol.* 2011;95:335-339.
8. Shah R, Shah S, Sengupta S. Results of small incision lenticule extraction: All-in-one femtosecond laser refractive surgery. *J Cataract Refract Surg.* 2011;37:127-137.
9. Hjortdal JO, Vestergaard AH, Ivarsen A, et al. Predictors for the outcome of small-incision lenticule extraction for Myopia. *J Refract Surg.* 2012;28:865-871.
10. Vestergaard A, Ivarsen AR, Asp S, et al. Small-incision lenticule extraction for moderate to high myopia: Predictability, safety, and patient satisfaction. *J Cataract Refract Surg.* 2012;38:2003-2010.
11. Wang Y, Bao XL, Tang X, et al. Clinical study of femtosecond laser corneal small incision lenticule extraction for correction of myopia and myopic astigmatism. *Zhonghua Yan Ke Za Zhi.* 2013;49:292-298.
12. Kamiya K, Shimizu K, Igarashi A, et al. Visual and refractive outcomes of femtosecond lenticule extraction and small-incision lenticule extraction for myopia. *Am J Ophthalmol.* 2014;157:128-134 e122.
13. Sekundo W, Gertner J, Bertelmann T, et al. One-year refractive results, contrast sensitivity, high-order aberrations and complications after myopic small-incision lenticule extraction (RelEx smile). *Graefes Arch Clin Exp Ophthalmol.* 2014.
14. Agca A, Demirok A, Cankaya KI, Yasa D, Demircan A, Yildirim Y, Ozkaya A, Yilmaz OF. Comparison of visual acuity and higher-order aberrations after femtosecond lenticule extraction and small-incision lenticule extraction. *Cont Lens Anterior Eye.* 2014;25(5):837-843.
15. Lin F, Xu Y, Yang Y. Comparison of the visual results after smile and femtosecond laser-assisted LASIK for myopia. *J Refract Surg.* 2014;30:248-254.
16. Dougherty PJ, Wellish KL, Maloney RK. Excimer laser ablation rate and corneal hydration. *Am J Ophthalmol.* 1994;118:169-176.
17. Mrochen M, Seiler T. Influence of corneal curvature on calculation of ablation patterns used in photorefractive laser surgery. *J Refract Surg.* 2001;17:S584-S587.
18. Schena E, Silvestri S, Franzesi GT, et al. Theoretical model and design of a device to reduce the influence of environmental factors on refractive surgery outcomes. *Conf Proc IEEE Eng Med Biol Soc.* 2006;1:343-346.
19. Reinstein DZ, Archer TJ, Gobbe M. Accuracy and reproducibility of cap thickness in small incision lenticule extraction. *J Refract Surg.* 2013;29:810-815.
20. Zhao J, Yao P, Li M, et al. The morphology of corneal cap and its relation to refractive outcomes in femtosecond laser small incision lenticule extraction (smile) with anterior segment optical coherence tomography observation. *PLoS One.* 2013;8:e70208.
21. Ozgurhan EB, Agca A, Bozkurt E, et al. Accuracy and precision of cap thickness in small incision lenticule extraction. *Clin Ophthalmol.* 2013;7:923-926.
22. Randleman JB, Dawson DG, Grossniklaus HE, et al. Depth-dependent cohesive tensile strength in human donor corneas: implications for refractive surgery. *J Refract Surg.* 2008;24:S85-89.
23. Scarcelli G, Pineda R, Yun SH. Brillouin optical microscopy for corneal biomechanics. *Invest Ophthalmol Vis Sci.* 2012;53:185-190.
24. Reinstein DZ, Archer TJ, Randleman JB. Mathematical model to compare the relative tensile strength of the cornea after PRK, LASIK, and small incision lenticule extraction. *J Refract Surg.* 2013;29:454-460.
25. Reinstein DZ, Archer TJ, Gobbe M. LASIK for myopic astigmatism and presbyopia using non-linear aspheric micro-ovision with the Carl Zeiss Meditec MEL 80 platform. *J Refract Surg.* 2011;27:23-37.
26. Reinstein DZ, Archer TJ, Gobbe M, et al. Corneal sensation after small incision lenticule extraction (smile). *J Refract Surg.* 2014 [In Press].
27. Wei S, Wang Y. Comparison of corneal sensitivity between FS-LASIK and femtosecond lenticule extraction (RelEx flex) or small-incision lenticule extraction (RelEx smile) for myopic eyes. *Graefes Arch Clin Exp Ophthalmol.* 2013;251(6):1645-1654.
28. Wei SS, Wang Y, Geng WL, et al. Early outcomes of corneal sensitivity changes after small incision lenticule extraction and femtosecond lenticule extraction. *Zhonghua Yan Ke Za Zhi.* 2013;49:299-304.
29. Vestergaard AH, Gronbech KT, Grauslund J, et al. Subbasal nerve morphology, corneal sensation, and tear film evaluation after refractive femtosecond laser lenticule extraction. *Graefes Arch Clin Exp Ophthalmol.* 2013;251:2591-2600.
30. Demirok A, Ozgurhan EB, Agca A, et al. Corneal sensation after corneal refractive surgery with small incision lenticule extraction. *Optom Vis Sci.* 2013;90:1040-1047.
31. Li M, Zhao J, Shen Y, et al. Comparison of dry eye and corneal sensitivity between small incision lenticule extraction and femtosecond LASIK for myopia. *PLoS One.* 2013;8:e77797.
32. Li M, Zhou Z, Shen Y, et al. Comparison of corneal sensation between small incision lenticule extraction (smile) and femtosecond laser-assisted LASIK for myopia. *J Refract Surg.* 2014;30:94-100.
33. Li M, Niu L, Qin B, et al. Confocal comparison of corneal reinnervation after small incision lenticule extraction (smile) and femtosecond laser in situ keratomileusis (FS-LASIK). *PLoS One.* 2013;8:e81435.

# First Experiences With SMILE

This 3<sup>rd</sup>-generation procedure is as safe and accurate as other methods of refractive surgery.

BY THOMAS F. NEUHANN, MD

Although I started performing SMILE less than 1 year ago, I have followed the development of the lenticule extraction principle of SMILE for much longer. I admit that, early on in the procedure's history, I questioned how removal of a refractive lenticule was a better strategy for refractive correction than reshaping the cornea with an ablative procedure—but I did see potential. Now that I have performed not only the first and second generations in laser vision correction (PRK and LASIK) but now also the 3<sup>rd</sup>-generation SMILE procedure for myself, I have seen more of this potential.

Initial results at the early level of development of ReLEx were intriguing; however, it still required flap creation (ReLEx FLEX) and, therefore, did not have much advantage over LASIK. The procedure became more appealing to me when the company introduced SMILE, because this is the closest thing to a purely intrastromal refractive surgery that is available today. The biggest advantage to working intrastromally to achieve a refractive correction is that the Bowman layer remains intact, thereby maintaining the mechanical stability of the cornea. Currently, the SMILE treatment is used for myopia corrections; however, other applications may be available in the future.

## INITIAL EXPERIENCE

I started performing SMILE in November 2013 and have treated approximately 50 patients to date (March 2014). Refractive results are astonishingly good and exact, and even my earliest patients have achieved visual acuities of 20/25 or better the day after surgery. Although this is about 1 line below the average after LASIK, ultimately vision is just as good with SMILE and it just takes a little longer to achieve.

In my experience, once patients learn about the biomechanical advantages of SMILE compared with LASIK, they are willing to wait the little extra time for visual quality to improve when openly and clearly informed about it.

Thus far, my patients have been happy with the results of this procedure, and they feel that their expectations have been fulfilled. With today's patients, who have extremely high expectations, this is an important aspect of the SMILE procedure.

## LEARNING CURVE

Like with any new procedure, there is a learning curve with SMILE. However, as an experienced corneal surgeon who has opened thousands of femtosecond laser flaps and implanted thousands of intracorneal ring segments, my learning curve was quite short. Even with the first cases, these patients did not have the slightest disadvantage or downside, other than the procedure took a few minutes longer because I had some difficulty achieving the second of two lamellar dissections.

The first dissection is performed between the cap and the top of the lenticule, and the second is performed underneath the lenticule. My advice to surgeons just starting out with SMILE is this: Try various instruments and practice on pig eyes until you find which suits you the best.

Personally, I currently prefer a short, thin spatula to open the dissection planes near the incision and a Seibel-type spatula for the dissection of the entire planes. I then grasp the lenticule with a pair of specialized forceps and pull it out.

## CONCLUSION

The biggest theoretical advantage of SMILE compared with LASIK is better biomechanical stability. Although I currently have results at 6-month follow-up only, other surgeons with longer-term follow-up have reported less regression and dry eye disturbances.<sup>1-3</sup> Time will tell if I have similar results, but currently I am more than pleased with my patients' initial outcomes. ■

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1. Xu Y, Yang Y. Dry eye after small incision lenticule extraction and LASIK for myopia. *J Refract Surg.* 2014;30:186-190.

2. Vestergaard AH1, Grønbech KT, Grauslund J, Ivarsen AR, Hjortdal JØ. Subbasal nerve morphology, corneal sensation, and tear film evaluation after refractive femtosecond laser lenticule extraction. *Graefes Arch Clin Exp Ophthalmol.* 2013;251:2591-2600.

3. Ivarsen A1, Asp S2, Hjortdal J. Safety and complications of more than 1500 small-incision lenticule extraction procedures. *Ophthalmology.* 2014;121:822-828.

# SMILE: My Refractive Surgery Procedure of Choice

This procedure is the most elegant form of keratomileusis.

BY EKKTET CHANSUE, MD

I performed my first LASIK procedure in 1994 using instrumentation designed for automated lamellar keratoplasty and the Aesculap-Meditec MEL 60 excimer laser (now Carl Zeiss Meditec). With each further development of microkeratomes and excimer lasers, LASIK became safer and more effective and accurate. Three years later, I cofounded TRSC International LASIK Center. It was the first dedicated, standalone refractive surgery center in Thailand. We started small and have grown to be the highest-volume refractive surgery center in the country, and we have performed more than 50,000 laser vision correction procedures to date.

Until 4 years ago, most of the refractive surgery procedures we performed were LASIK, but we have now shifted our procedure of choice, especially for primary myopic cases, to SMILE performed with the ZEISS VisuMax femtosecond laser.

## SMILE: A MAJOR PARADIGM SHIFT

I learned about ReLEx several years ago, but I was not impressed by the earliest development ReLEx FLEx because it involved lifting the flap in almost the same fashion as LASIK. The refractive results with ReLEx FLEx were similar to LASIK results, but visual recovery was slower. Therefore, I did not see its potential to make any significant difference in postoperative outcomes.

However, in March 2009, at a core ZEISS Refractive Faculty Meeting in Hong Kong, I had one of the most significant moments of my professional life. During a talk by Rupal S. Shah, MD, she played a video depicting the latest advancement of the ReLEx technique—SMILE. When she extracted the lenticule through a few millimeters' worth of incision, I almost fell off my chair: I realized I was witnessing the start of a major paradigm shift in refractive surgery. This new technique was the most elegant implementation of Professor Barraquer's keratomileusis that I had ever seen, and I decided that I needed to adopt this procedure immediately.

## EARLY ADOPTER OF THE PROCEDURE

My desire to transition to SMILE from LASIK was

strengthened during my visit to Dr. Shah's practice in Vadodara, Gujarat, India. I was completely sold on the procedure when she showed me postoperative topographies of eyes with extremely wide areas of curvature change (ie, large effective optical zones) in relatively high corrections—something I almost never saw in LASIK.

I became one of the early adopters of the SMILE procedure in 2010, as I practice in one of the study sites that was involved in the premarket evaluation. The past 4 years have proven to me that SMILE delivers on all of its promises; this solution is every bit as efficacious, safe, and accurate as LASIK, with the added benefits of increased corneal strength, great uniform corneal curvature that causes almost no night vision complaints, and fewer dry eye symptoms. Surely there have been kinks along the way, such as the need for new instruments and techniques; however, within 6 months of adopting the new treatment, the proportion of SMILE to LASIK procedures we were performing continued to grow.

The microincisional nature of the procedure resonates with patients' predilections and with the general trend of medicine heading toward minimally invasive surgery. I consult with prospective patients the same way I always have, the only exception being that I now include SMILE on our treatment list. I make a clear distinction between the facts and theoretical benefits of this procedure and let the patient decide if the treatment is right for him or her. Most of the time, my patients choose SMILE.

## ENHANCEMENTS WITH THE CIRCLE TECHNIQUE

Our enhancement rate for SMILE is roughly the same as with LASIK. This is not reflective of the procedure as much as it is patients' visual progressions over time. Visual needs change, and often patients require some adjustment in their vision; there is also the natural progression of myopia that occurs in some patients. As a surgeon continues to follow patients for 10 to 20 years, he or she will find that these patients' needs for enhancement surgery rise. Therefore, a procedure that is adjustable will be more likely to prevail. In my view, LASIK owes its success to the fact that the results can

be relatively easily modified and the patient can return to work the next day.

With SMILE, however, enhancements are a bit different. Ideally, the touch-up surgery should leave the eye in roughly the same condition as it was preoperatively—namely, flapless and only with a microincision. The ideal enhancement procedure would create another lenticule for extraction using the same entrance wound and intrastromal pocket as the original surgery. However, current technology cannot accurately identify the original pocket in three-dimensional coordinates in order for the femtosecond laser to create another lenticule cut.

This necessitates the need to resort to the excimer laser for enhancement. For this, the surgeon must either make a flap in order to perform LASIK or perform a surface treatment.

I consider either option as defeating the main advantage of SMILE, which is an intact anterior stroma. With that said, when an enhancement after SMILE is necessary, I lean toward doing a flap-based procedure. ZEISS has developed the CIRCLE program, which basically turns the SMILE procedure into femtosecond LASIK. We have done about 60 enhancements using this software, and it has worked flawlessly. Hopefully CIRCLE is an interim option for more elegant ways to enhance a previous treatment with SMILE.

## CONCLUSION

I believe that, after PRK and LASIK, SMILE is the 3<sup>rd</sup> generation in laser vision correction. It will substitute for LASIK as the refractive procedure of choice in mainstream refractive surgery sometime in the distant future, as it represents a natural progression toward minimally invasive medicine.

This paradigm shift will take time, however, as LASIK continues to produce great results and has an enormous base of manufacturers of instruments and equipment. There are hundreds of combinations of microkeratomes, femtosecond lasers, and excimer lasers that a surgeon can use to perform LASIK. In contrast, SMILE is performed only with the VisuMax femtosecond laser. Inevitably, there might be other lasers capable of performing refractive cuts like the VisuMax and, therefore, the 3<sup>rd</sup> generation in laser vision correction SMILE. However, as of 2014, there seems to be none on the horizon. ■

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1. Barraquer JJ. Queratoplastia Refractiva. Estudios e Informaciones. *Oftalmologicas*. 1949;2:10-30.
2. Barraquer JJ. Modification of refraction by means of intracorneal inclusions. *Int Ophthalmol Clin*. 1966;6(1):53-78.



# Convincing Results With SMILE

The 3<sup>rd</sup> generation in laser vision correction is well established only 3 years after market introduction.

BY OSAMA IBRAHIM, MD; AHMED EL-MASSRY, MD; AMR SAID, MD; MOONES ABDALLA, MD; AND IBRAHIM OSAMA, MD

Today, two laser systems are commonly used in LASIK: a femtosecond laser to fashion a corneal flap and an excimer laser to perform the corneal ablation.<sup>1</sup> More recently, however, refractive lenticule extraction (SMILE; Carl Zeiss Meditec) was introduced as a laser vision correction procedure that does not require the use of an excimer laser.

## OVERVIEW OF THE ADVANTAGES

SMILE is a minimally invasive, flapless procedure that reduces surgical time and corneal biomechanical changes<sup>2</sup> and avoids flap-related complications including free caps, buttonholes, irregular cuts, wrinkled flaps, striae, and diffuse lamellar keratitis (DLK).<sup>3,4</sup> It requires a small sidecut incision, 3 to 4 mm wide, in the anterior cornea. In addition to causing fewer biomechanical changes than a 20- to 25-mm LASIK flap sidecut, the cut required in SMILE produces less reduction of trigeminal nerve density and less severe postoperative dry eye symptoms.

Another advantage of SMILE appears in patients with high refractive errors. In conventional LASIK, the higher the error the longer the ablation time; however, in SMILE, the time for lenticule creation is almost consistent, regardless the preoperative refraction.<sup>5</sup>

## TREATMENT AND PARAMETERS

We started using SMILE in 2010. Collectively, we have performed this treatment in 1,100 patients, of whom 120 (220 eyes) have completed 3-year follow-up. Seventy participants are women and 50 are men; of these, 89 are previous contact lens wearers. Their mean age is  $25 \pm 4.5$  years. Results of this study are described in detail below.

In every case, we made a 90- $\mu$ m cap and 3-mm incision at 120°, through which the lenticule was removed. The optical zone varied from 5.5 to 6.5 mm, according to the patient's corneal thickness and refractive error, and the minimum extra lenticule thickness forming the edge of the lenticule was 10  $\mu$ m.<sup>6</sup>

We used disposable treatment packs, sized in small and medium, that consist of a curved contact glass and a filter attached to the contact glass by a connecting hose; we selected the smallest possible treatment pack

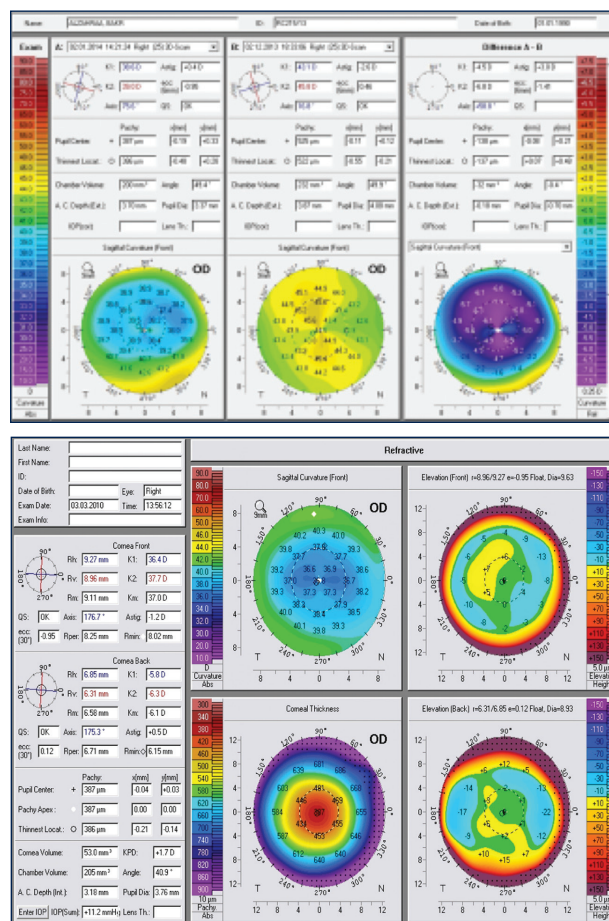


Figure 1. Top: Pentacam comparison map of before and after SMILE. Bottom: Pentacam map of a patient undergoing SMILE.

to minimize intraoperative suction loss risk. The diameter of suction was chosen to be slightly less than the white-to-white (WTW) corneal diameter. For medium treatment packs, the minimum recommended WTW corneal diameter was 12 mm.

The procedure was done under topical anesthesia, and both eyes were sterilized with bovidone iodine and draped before initiating surgery. Careful placement and inspection of the contact glass was carried out to ensure proper centration. However, optical lenticule design is forgiving for minor decentrations in this myopic cases.





**Figure 2.** Mean spherical equivalent before surgery and 1 month, 6 months, 1 year, 2 years, and 3 years after surgery.

The VisuMax femtosecond laser (Carl Zeiss Meditec) was used to create the lenticule and the incision. Upon completion of both, the patient was released automatically from the contact glass. The access incision was opened and the lenticule was dissected using a spatula. The lenticule was then removed using a special forceps. Intraoperative suction loss due to patient movement occurred in five patients who underwent surgery on the same day, with the same technique.

Postoperatively, topical antibiotics (moxifloxacin), steroids (prednisolone), and artificial tears were prescribed every hour during the first day. Antibiotics and steroid doses were titrated to every 4 hours for 7 days only, and the use of artificial tears was continued every 4 hours for about 1 month.

## RESULTS

Figure 1 shows Pentacam (Oculus Optikgeräte) maps of patients undergoing SMILE. The most important outcomes were identified as improved mean spherical equivalent and BCVA.

**Spherical equivalent.** Mean spherical equivalent improved from  $-8.50 \pm 1.50$  D preoperatively to  $-1.80 \pm 0.40$  D at 1 month,  $-1.20 \pm 0.40$  D at 1 year,  $-1.30 \pm 0.40$  D at 2 years, and  $-1.30 \pm 0.54$  D at 3 years (Figure 2).

**BCVA.** Mean BCVA improved from  $0.70 \pm 0.76$  preoperatively to  $0.90 \pm 0.22$  at 3 years postoperatively, and mean UCVA was  $0.8 \pm .43$  at 3 years postoperatively.

**Postoperative complications.** At each follow-up visit (1 week; 1 month; and 1, 2, and 3 years), all patients were asked about dry eye symptoms and night vision problems. Even though at the 1-week visit 100 patients (83%) reported dry eye symptoms, the figure dropped on subsequent visits. After 1 month, only 30 (25%) reported problems with dry eye and, after 1 year, only 6 patients (0.5%) continued to have symptoms necessitating the use of lubricating eye drops. At 1 week,

1 month, and 3 years, 60 (50%), 20 (16%), and two (0.16%) patients, respectively, reported night vision problems.

Postoperative pain due to epithelial erosion occurred in three patients. Topical medications were prescribed and a bandage contact lens was placed; in all cases, the epithelial erosion cleared up within 3 days of surgery. No postoperative infection, ectasia, DLK, or epithelial ingrowth were reported in our cases.

## CONCLUSION

SMILE is a safe, effective, and predictable refractive procedure that has the potential to replace conventional refractive surgery procedures such as LASIK. The advantage is greatest in eyes with high refractive errors. Additionally, we expect for more advances in this flapless technique to emerge, giving us further options for customized treatments and touch-up procedures. ■

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1. Salomao MQ, Wilson SE. Femtosecond laser in situ keratomileusis. *J Cataract Refract Surg.* 2010;36:1024-1032.
2. Roberts C, guest ed. Special issue on corneal biomechanics. *J Cataract Refract Surg.* 2005;31(1).
3. Kim P, Sutton GL, Rootman DS. Applications of the femtosecond laser in corneal refractive surgery. *Curr Opin Ophthalmol.* 2011;22:238-244.
4. Sekundo W, Kunert K, Russmann C, et al. First efficacy and safety study of femtosecond lenticule extraction for the correction of myopia: Six-month results. *J Cataract Refract Surg.* 2008;34:1513-1520.
5. Hovanesian JA, Shah SS, Maloney RK. Symptoms of dry eye and recurrent erosion syndrome after refractive surgery. *J Cataract Refract Surg.* 2001;27(4):577-584.
6. Lubatschowski H. Overview of commercially available femtosecond lasers in refractive surgery. *J Refract Surg.* 2008;24:S102-S107.

# Biomechanical Effects of LASIK Flaps and SMILE Caps

A virtual clinical study confirmed the hypothesis that a cap induces less central flattening and leaves the cornea with greater biomechanical strength than a flap.

BY HARALD P. STUDER, PhD; AND CYNTHIA J. ROBERTS, PhD

With about 700,000 procedures performed each year in the United States alone, LASIK is the most common refractive surgical procedure for the correction of myopia and hyperopia. Even though it is a well-established procedure with a high success rate, it has several disadvantages, and commonly listed side effects include surgically induced dry eye and over- or undercorrection. Additionally, postoperative biomechanical decompensation resulting in corneal ectasia can occur; however, this is relatively rare.

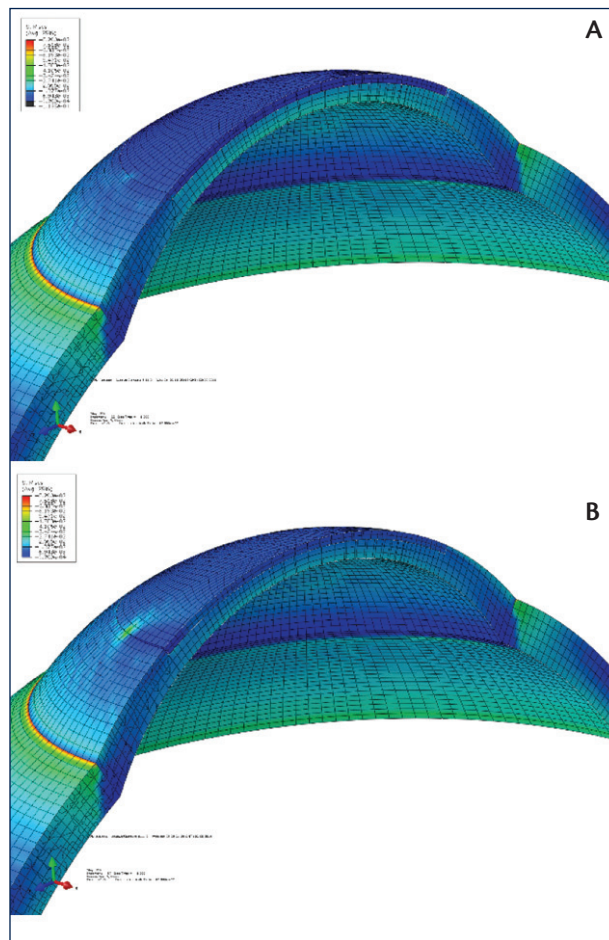
The less-invasive, femtosecond-laser-based SMILE solution (Carl Zeiss Meditec) may address some of these issues. Its most apparent distinction from LASIK is that tissue removal is no longer achieved via excimer laser ablation, but rather dissection with the femtosecond laser. The refractive lenticule, as it is called, is manually removed through a small keyhole incision located anteriorly on the cornea.

Because SMILE does not require a flap cut, it was hypothesized that less central corneal flattening and biomechanical weakening would be induced by the procedure. In order to rigorously test these theoretical assumptions, we conducted a comparative in-silico parametric study. Simulations and comparisons were confined to the effects of the LASIK flap and the SMILE cap only (ie, without tissue removal), as the LASIK ablation and the lenticule extraction can be considered biomechanically similar because they remove the same amount of tissue. The comparison of stress pre- and postoperatively is cleaner if the thickness has not changed. In other words, the stress would be different after surgery than it was before surgery, simply due to the change in thickness.

The aim of our study was to show the difference in stress with a SMILE cut compared with a LASIK flap, without the added complexity of a change in thickness.

## METHODS

This numerical study was designed to analyze the corneal shape changes and biomechanical impacts of SMILE and LASIK with respect to the following flap/cap parameters: diameter, depth, and length (flap hinge and cap keyhole incision). The parameter combinations of three



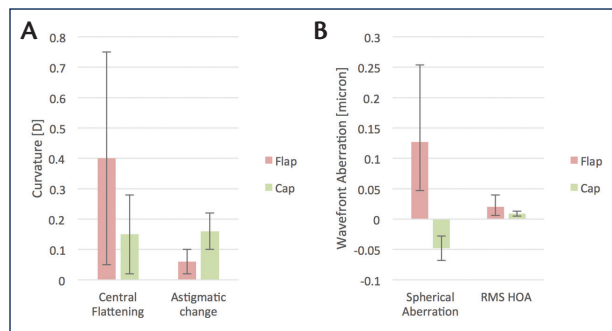
**Figure 1.** Finite element models of a LASIK flap (A) and SMILE cap (B). The models were cut in half for illustration purposes; full 360° models were used in the simulation.

diameters (7, 8, and 9 mm), three depths (90, 120, and 180  $\mu\text{m}$ ), and two hinge/incision lengths (3 mm and 90° arc-length) lead to 18 simulations for the SMILE cap and 18 for the LASIK flap.

Numerical simulations were carried out using the finite element method and a custom mathematical function describing the mechanical behavior of human corneal tissue. The function considered the tissues' incompressibility and nonlinearity, the fiber-induced anisotropy, and



**Figure 2.** Comparison of stress distribution in the stromal bed below the SMILE cap and LASIK flap. The cap cuts almost maintain the preoperative stress distribution (green), but the flap cuts induce significant additional stress into the stromal bed (purple).



**Figure 3.** Surgically induced change in corneal shape (A) and function (B) for LASIK flap and SMILE cuts. Except for some higher values for induced astigmatism, the cap is more neutral than the flap cut.

the inhomogeneity over the depth-profile. All 36 simulation models were first prepared in the Optimeyes software (Integrated Scientific Services) and then calculated with the ABAQUS 6.11-3 finite element solver (Dassault Systèmes).

## RESULTS

Sample finite element models for the flap and cap are shown in Figure 1. Mean surgically induced central flattening (central 4 mm diameter) for the LASIK flap and SMILE cap simulations were  $-0.40 \pm 0.35$  D (standard deviation; SD) and  $-0.15 \pm 0.13$  D (SD), respectively (Figure 2).

Surgically induced spherical aberration was in line with central flattening, showing higher values for the flap simulations ( $-0.127 \pm 0.08$   $\mu$ m [SD]) than for the cap simulations ( $-0.048 \pm 0.02$   $\mu$ m [SD]; Figure 3). On the other hand, the flap induced comparably low astigmatic changes ( $0.06 \pm 0.04$  D [SD]) and the cap simulations induced  $0.31 \pm 0.21$  D (SD; Figure 3). However, when we analyzed

only the cap simulations with 3-mm keyhole incisions ( $n=9$ ), the mean induced astigmatism dropped to  $0.16 \pm 0.06$  D (SD). Shallower caps of 90  $\mu$ m also induced less astigmatic change ( $0.19 \pm 0.10$  D). Further, the flap simulations induced greater total higher-order aberrations ( $0.020 \pm 0.014$   $\mu$ m [SD]) than the cap simulations ( $0.009 \pm 0.004$   $\mu$ m [SD]), although both are quite low (Figure 3).

Biomechanical analysis showed the preoperative central stroma with a stress of 12.6 kPa. Stresses increased to  $13.3 \pm 0.9$  kPa (SD) after the cap cuts and to  $16.2 \pm 1.8$  kPa (SD) after the flap cuts. This corresponds to an increase in stromal stress of 6% and 29% for SMILE cap and LASIK flap, respectively.

## DISCUSSION

The results of this numerical parametric study confirmed the initial hypothesis that the SMILE cap induces considerably less central flattening and leaves the cornea with greater biomechanical strength than the LASIK flap. The small amounts of surgically induced astigmatism in both procedures are likely clinically insignificant.

Generally it can be said that SMILE is biomechanically a more stable procedure than LASIK, as it maintains the integrity of the anterior cornea. As a result, SMILE may have the potential for deep refractive surgical interventions. ■

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# Correction of Low Myopia

Is SMILE a good procedure for treating this common refractive error?

BY SRI GANESH, MBBS, MS, DNB

LASIK and surface ablation are the preferred techniques for correction of low myopia, and both give patients excellent results. Although the newly introduced SMILE technique for treatment of myopia has been shown to be effective and stable for moderate and high myopia, there is some trepidation in treating low myopia with this technique. The various reasons for concern are accuracy in creating, dissecting, and handling a thin lenticule; tearing of a thin lenticule during extraction; and whether the procedure has the same *wow factor* and recovery as LASIK or PRK. However, we treated a series of patients with low myopia, and the outcomes were excellent stability and patient comfort and satisfaction.

## STUDY

We prospectively studied 153 eyes of 82 patients with low myopia (range, -0.75 to -3.00 D spherical equivalent) and analyzed the visual and refractive outcomes 3 months after SMILE. The mean age of patients was  $25.43 \pm 3.20$  years, and the mean preoperative spherical equivalent was  $-1.98 \pm 0.55$  D. The surgical technique was uniform, and every parameter except the optical zone was fixed.

Using the VisuMax femtosecond laser (Carl Zeiss Meditec), a refractive lenticule was created according to the myopic error, with a SMILE cap thickness of 100  $\mu$ m, optical zone varying from 6 to 6.5 mm, and a superior 2-mm incision. Minimum residual bed thickness was 280  $\mu$ m, and the minimum peripheral thickness of the lenticule was 15  $\mu$ m. Both planes of the lenticule were dissected and removed manually, followed by washing of the interface with balanced saline solution.

Suction loss occurred in two eyes, of which one was redocked and treated with SMILE and the other required conversion to a flap-based procedure with an excimer laser. Additionally, one eye had extension of the incision (ie, cap tear) and two eyes had a small peripheral lenticular tear due to dense peripheral opaque bubble layer.

Postoperatively, all corneas were clear, with no subconjunctival hemorrhage, haze, or interface problems. Patients were comfortable and did not report any significant visual symptoms. On day 1, 89.3% of eyes had achieved 6/6 UCVA and 7.7% had better than 6/6, which improved to 64.3% at the end of 3 months. Also at 3 months, 98.8% of eyes had 6/6 or better BCVA and

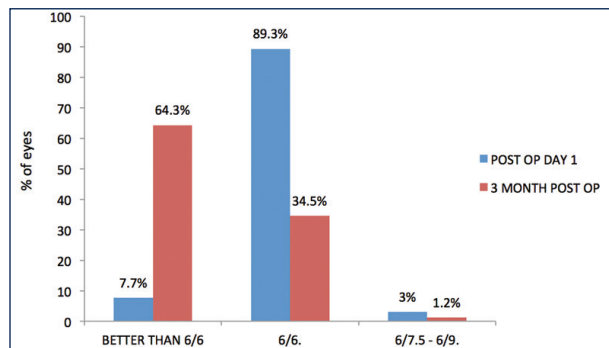


Figure 1. BCVA on postoperative day 1 and month 3.

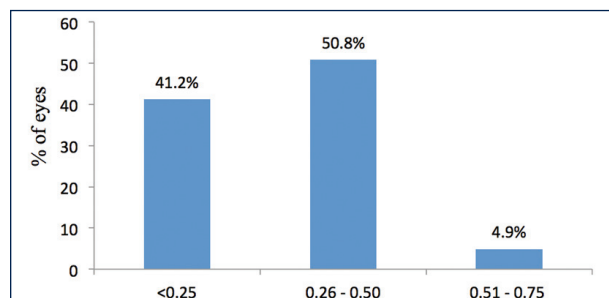


Figure 2. Postoperative residual refraction in diopters.

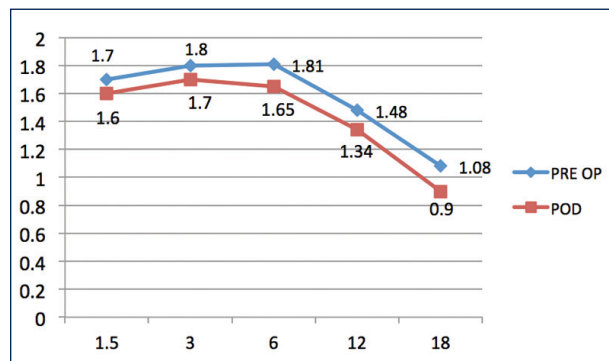


Figure 3. Pre- and postoperative (3 months) functional acuity contrast sensitivity ( $P=.126$ ).

only 1.2% had vision that was less than 6/6. No eye had loss of BCVA postoperatively (Figure 1).

The residual refraction in 92% eyes was within  $\pm 0.50$  D spherical equivalent and only 4.9% were in the range of  $\pm 0.50$  to 0.75 D spherical equivalent (Figure 2). We observed an initial and significant drop in the functional acuity contrast sensitivity in all patients on postoperative day 15 ( $P<.05$ ), but all patients showed improvement by 3 months ( $P=.126$ ; Figure 3).

There was no significant difference in dry eye status



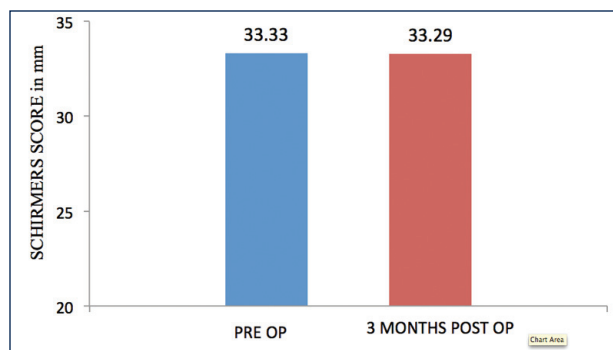


Figure 4. The prevalence of dry eye before surgery and 3 months postoperatively.

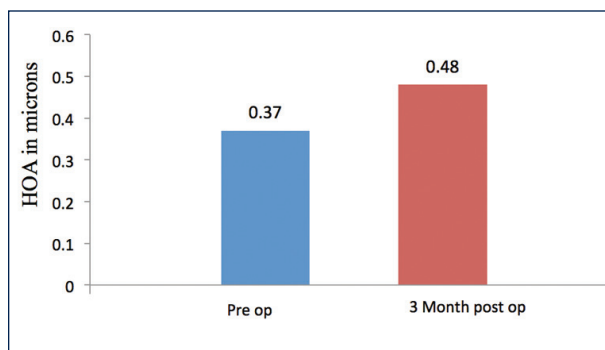


Figure 5. The presence of higher-order aberrations before surgery and 3 months postoperatively.

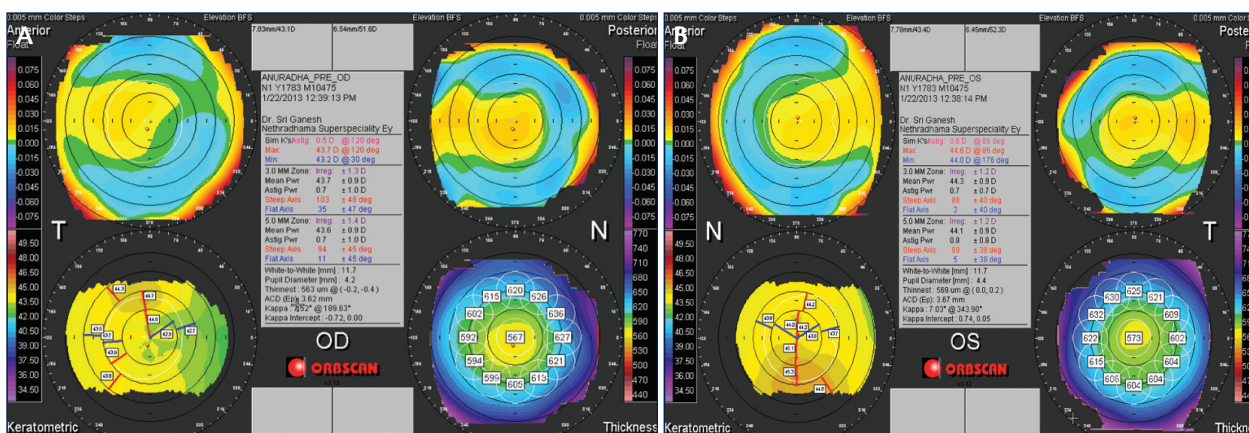


Figure 6. Preoperative topography of a patient's right (A) and left (B) eyes.

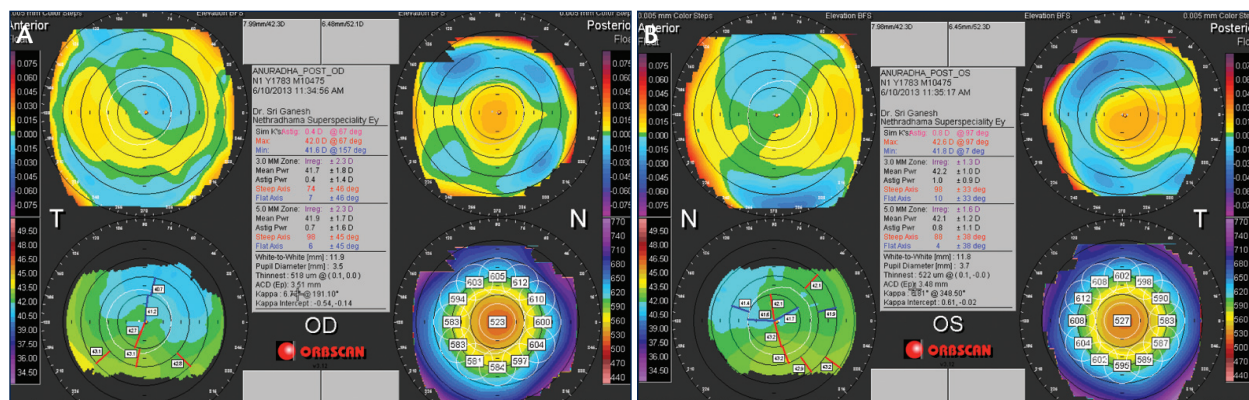


Figure 7. The 3-month postoperative topography of the right (A) and left (B) eyes in the same patient in Figure 6.

pre- and postoperatively (Figure 4); however, there was mild increase in higher-order aberrations at 3 months, which was not significant ( $P < .05$ ; Figure 5).

Figure 6 shows an example of a patient who underwent SMILE for -2.25 D of myopia in the right eye and -2.00 D in the left. Postoperatively, the patient had a UCVA of 6/5 in both eyes (Figure 7).

## CONCLUSION

The flapless SMILE procedure makes minimally invasive refractive correction possible. It produces excellent visual results, even in lower degrees of myopia (as low as -0.75 D spherical equivalent), with excellent stability and patient

comfort and satisfaction. Although there was an initial drop in contrast sensitivity, this improved by 3 months.

In my experiences, SMILE has the safety profile of PRK and the comfort and wow factor of LASIK, and thus has become my preferred choice to correct myopia and myopic astigmatism. ■

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# Preserving Corneal Neural Architecture

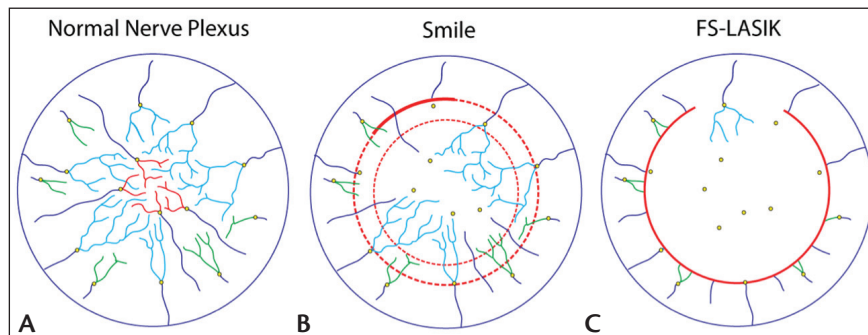
SMILE has good postoperative corneal sensitivity and can reduce the incidence and course of postoperative ocular surface symptoms.

BY LEONARDO MASTROPASQUA, MD; AND MARIO NUBILE, MD

**D**ry eye symptoms and related epitheliopathy occur commonly after traditional refractive surgery techniques. The most reported manifestation is ocular dryness, which occurs in almost 40% of eyes treated with LASIK and PRK, followed by nonspecific ocular surface discomfort and sharp pain when waking.<sup>1</sup> Changes in corneal shape, tear film dynamics, and subepithelial innervation after surgery may play a role in the onset of ocular discomfort, and impact of these factors may be detrimental to visual quality.<sup>2</sup>

It is well known that excimer-laser-based procedures result in sudden central corneal nerve fiber damage. In LASIK, this is related to the flap cut; in PRK, the excimer photoablation of the stroma containing nerve fibers. The wound-healing response (ie, time-to-recovery and morphological appearance of the regenerated nerve plexus) in the central corneal subepithelial nerves is only slightly different between LASIK and similar flap-based procedures.<sup>3</sup> Regardless, postoperative nerve density and morphology remain altered for years after surgery, explaining some clinical conditions of dryness and recurrent superficial epithelial punctate erosions.

Corneal sensitivity follows a similar pattern by declining in the first 3 months and returning to normal values between 6 and 12 months after excimer-based surgeries.<sup>4,5</sup> LASIK retrieved worse results in terms of corneal sensitivity, tear break-up time, Schirmer test values, and corneal re-innervation than LASEK and PRK at 6 months. The introduction of flap creation with the femtosecond laser improved the reliability of LASIK by setting up planar configuration of the flap cut geometry,<sup>6</sup> nevertheless, corneal nerve plexus is severely damaged



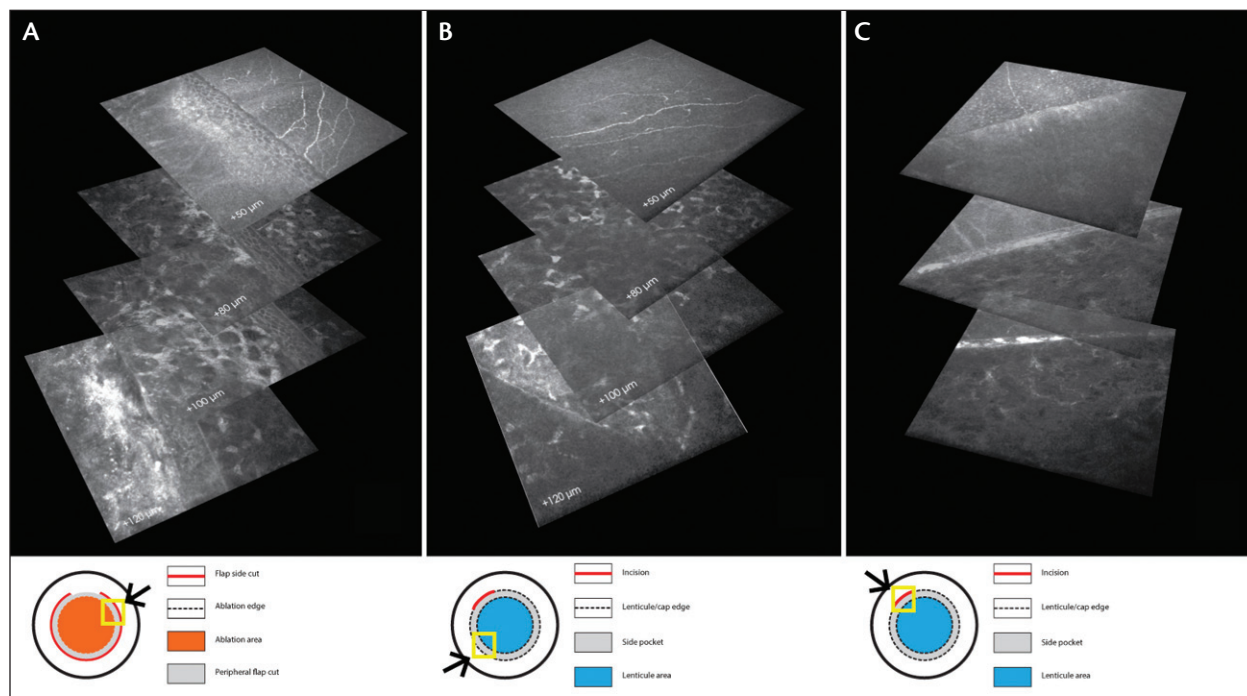
**Figure 1.** Stromal nerve fiber bundles run centripetally and toward the surface, perforating the BL (A; spots indicated by yellow circles). Once the fibers penetrate the BL, the subbasal nerve plexus is originated (perforating stromal fibers: central = red, paracentral = light blue, and peripheral = green). In the absence of a full flap sidecut, as with SMILE, peripheral nerve fibers are resected only where the 50° arc of the incision is placed (B; thick red line) and if rising superficially to perforate the BL within the area of the created and extracted refractive lenticule. The other fibers that had penetrated the BL outside the lenticule area may run undisturbed as subbasal nerve plexus. (For simplicity, central subbasal surviving fibers are not depicted in the central zone). During femtosecond LASIK, all fibers are cut throughout the extension of the 300-310° degree of arc flap sidecut; moreover, all deeper fibers are disrupted within the photoablation area (C).

for a long time, as flap creation implies the transection of all nerve fibers at the lamellar border. Therefore, the planar configuration of thin-flap LASIK does not seem to be associated with clinically significant advantages in terms of induced neurotrophic epitheliopathy.

Femtosecond laser refractive surgery underwent a big advancement with the introduction of SMILE (Carl Zeiss Meditec). With this flapless procedure, corneal tissue removal is achieved by creating a dissection lenticule and a small incision from which it is extracted. Two dissection planes are produced: one to design the backside of the lenticule and the other to create the anterior face, which is enlarged to form a side pocket dissection plane for later extraction maneuvers. The procedure does not affect the superficial tissue, fashioning an intrastromal disc that can be extracted through the small incision.

## PRESERVE MORE NERVE FIBERS

The basis that explains the nerve fiber resection induced by SMILE or other refractive surgical procedure



**Figure 2.** Sidecut IVCM stack reconstruction: Femtosecond LASIK (A), SMILE peripheral lenticule edge (B), SMILE incision (C). The top panel in Figure 2A shows resected fibers at the flap border 1 week after surgery; underlying panels show deeper stromal layers. The top panel in Figure 2B shows the untouched superficial fibers; the bottom panel shows these running over the lenticule stromal edge. The top panel in Figure 2C shows that the small incision represents a zone of superficial nerve fiber resection in the SMILE technique.

relies in the understanding of the intracorneal distribution of the nerve fibers that give origin to the subbasal nerve plexus. Corneal nerve anatomy was recently revisited by Al-Aqaba and Dua, who demonstrated that stromal nerves penetrate the Bowman layer (BL) at different locations, mostly those situated in the mid-peripheral zone, creating the subbasal plexus.<sup>7</sup>

Figure 1A is a schematic illustrating the nerve fiber pathway. It is reasonable to hypothesize that, when a flap-based technique such as LASIK or femtosecond LASIK (femto-LASIK) is performed, all nerve fibers that run within the flap sidecut—the vast majority of the fibers—are resected (Figure 1C). This hypothesis explains the marked reduction of the central subbasal corneal nerve plexus after LASIK. With SMILE, however, it is presumed that some fibers are resected due to the sidecut/incision and because of the interruption of fibers perforating the Bowman zone inside the refractive lenticule and cap area. Conversely, fibers that gained the superficial subepithelial location after perforating the BL in areas outside of the lenticule may run undisturbed over the refractive zone, with the exception of the mentioned peripheral incision (Figure 1B).

Evaluations of corneal innervation and corneal sensitivity after ReLEx techniques have shown that corneal sensitivity was significantly better after SMILE than after LASIK,<sup>8</sup> and central subbasal nerve plexus morphology

is less affected by the SMILE procedure than it is by the ReLEx FLEX technique.<sup>9</sup> Li et al<sup>10</sup> also reported better preservation of nerve morphology and density in eyes treated with SMILE versus femto-LASIK.

### REMARKABLE DIFFERENCES

We have observed remarkable differences between the induced alterations and corneal nerve wound-healing patterns of femto-LASIK and SMILE for similar myopic corrections.

When studying the peripheral nerve fiber integrity in the areas corresponding to the flap sidecut in LASIK and the lenticule in SMILE with laser-scanning in vivo confocal microscopy (IVCM), we noticed that all centripetally running fibers were resected by the presence of a sidecut (Figure 2). In femto-LASIK, the fibers are circumferentially interrupted throughout the extension of the flap cut at the time of surgery. Additionally, ablation of the central stroma may contribute to the damage to deeper fibers (Figure 2A). With SMILE, peripheral fibers were observed running centripetally and nonresected in the area overlying the edge of the lenticular lamella (Figure 2B). Similarly to LASIK, the fibers are resected where the incision required of SMILE is placed (Figure 2C).

Combined, the peripheral transection of the nerve fibers and the use of a central ablation in LASIK explain that, starting from 1 week postoperatively, central nerve



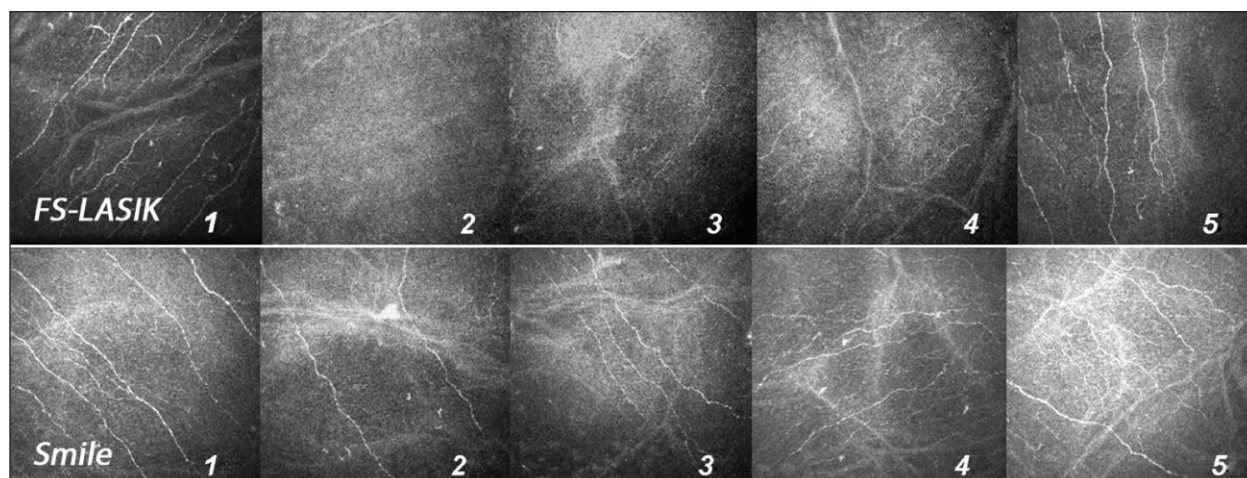


Figure 3. In vivo confocal microscopy images of the central subbasal nerve plexus before and after femtosecond LASIK (top row) and SMILE (bottom row). In each row, 1 =preoperative, 2 = 1 week; 3 = 1 month; 4 = 3 months; 5 = 6 months. Note that viable fibers are visible at 1 week and 1 month after surgery in the SMILE group; partial recovery of nerve fiber density starts 3 months after LASIK.

fiber density is markedly reduced (up to 95% of the preoperative values). Several months are generally necessary to observe a partial recovery of the fiber density. Conversely, in the SMILE technique, we found that the reduction in nerve fiber density was significantly less than in LASIK at each time point in follow-up. Additionally, central re-nervation was faster than in LASIK and approximately 30% of the central fibers were spared by the procedure. Central nerve fibers were detectable at 1 week after SMILE (Figure 3), and a rapid gain of central nerve fiber density was observed.

The main reason for the nerve-sparing characteristic of SMILE may be due to the absence of a sidecut that transects all edge-crossing fibers. The respect of superficial subbasal nerve plexus may play a role in maintaining a partial corneal innervation in the early postoperative period and may be also responsible for the rapid nerve regrowth observed in the first months after surgery. (Figure 3).

## CONCLUSION

All these findings suggest that SMILE better preserves the corneal neural architecture and has greater post-operative corneal sensitivity when compared with flap-based techniques such as LASIK. This favorable condition is likely to reduce the incidence and course of postoperative ocular surface symptoms and dry-eye-related epitheliopathy in patients. ■

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1. Hovanesian JA, Shah SS, Maloney RK. Symptoms of dry eye and recurrent erosion syndrome after refractive surgery. *J Cataract Refract Surg*. 2001;27(4):577-584.
2. Ambrósio R Jr, Tervo T, Wilson SE. LASIK-associated dry eye and neurotrophic epitheliopathy: pathophysiology and strategies for prevention and treatment. *J Refract Surg*. 2008;24(4):396-407.
3. Zhang F1, Deng S, Guo N, et al. Confocal comparison of corneal nerve regeneration and keratocyte reaction between FS-LASIK, OUP-SBK, and conventional LASIK. *Invest Ophthalmol Vis Sci*. 2012;53(9):5536-5544.
4. Pérez-Santonja JJ, Sakla HF, Cardona C, et al. Corneal sensitivity after photorefractive keratectomy and laser in situ keratomileusis for low myopia. *Am J Ophthalmol*. 1999;127(5):497-504.
5. Murphy PJ, Corbett MC, O'Brart DP, et al. Loss and recovery of corneal sensitivity following photorefractive keratectomy for myopia. *J Refract Surg*. 1999;15(1):38-45.
6. Patel SV, McLaren JW, Kittleson KM, et al. Subbasal nerve density and corneal sensitivity after laser in situ keratomileusis: femtosecond laser vs mechanical microkeratome. *Arch Ophthalmol*. 2010;128(11):1413-1419.
7. Al-Aqaba MA, Fares U, Suleman H, et al. Architecture and distribution of human corneal nerves. *Br J Ophthalmol*. 2010;94(6):784-789.
8. Wei S, Wang Y. Comparison of corneal sensitivity between FS-LASIK and femtosecond lenticule extraction (ReLEx flex) or small-incision lenticule extraction (SMILE) for myopic eyes. *Graefes Arch Clin Exp Ophthalmol*. 2013;251(6):1645-1654.
9. Vestergaard AH, Grønbech KT, Grauslund J, et al. Subbasal nerve morphology, corneal sensation, and tear film evaluation after refractive femtosecond laser lenticule extraction. *Graefes Arch Clin Exp Ophthalmol*. 2013;251(11):2591-2600.
10. Li M, Niu L, Qin B, et al. Confocal comparison of corneal reinnervation after small incision lenticule extraction (SMILE) and femtosecond laser in situ keratomileusis (FS-LASIK). *PLoS One*. 2013;8(12):e81435.



# SMILE for Hyperopic Corrections

Early results show no signs of regression at 3 months postoperatively.

AN INTERVIEW WITH WALTER SEKUNDO, MD

*In vivo findings in an animal model suggest that surgical denervation after SMILE is significantly less than after flap-based refractive surgery and, therefore, is associated with quicker nerve regeneration.<sup>1</sup> Also confirmed by several clinical studies,<sup>2-9</sup> these results could mean better preservation of the corneal neural architecture and reduced dry eye symptoms in treated patients. This treatment has also been shown to have a similar safety profile and postoperative outcomes as LASIK.<sup>2,3</sup>*

*A recent study of SMILE in patients with myopia and myopic astigmatism showed promising treatment outcomes at 1 year, with 88% of eyes that had a plano target achieving distance UCVA of 20/20 or better, a mean spherical equivalent of  $-0.19 \pm 0.19$  D, and insignificant changes in mean refraction between 1 and 12 months (0.08 D) and in mesopic and photopic contrast sensitivity.<sup>10</sup>*

*In the second phase of this research, Walter Sekundo, MD, Marcus Blum, MD, and colleagues are studying the use of lenticule extraction using FLEX method for hyperopic corrections. Initial results have confirmed the potential for further development of previous solution of the flap-free solution for refractive corrections other than myopia. In the interview below, Professor Sekundo reviews the 3-month results.*

## Question No. 1: What is the design of the ReLEx FLEX hyperopia study?

Answer: We first designed the study with a rather simple hyperopic profile; however, the major problem was that a substantial regression occurred over time. Although 1-month results were good, by 3 months, about 33% of patients showed signs of regression and, by 6 months, about 50% of patients had regressed.<sup>11</sup> After consulting with the Carl Zeiss Meditec research team, we asked them to develop profiles with a larger transition zone, similar to the current treatment algorithms of the MEL 80 and MEL 90 excimer lasers. We then refined the study and used more sophisticated hyperopic profiles. To date, nine eyes of five patients have been treated with this new profile (Figure 1).

Unlike the first study, results have been much better,

and we investigators are confident that the early trend in this study will carry on.

## Question No. 2: How did you select patients for enrollment?

Because the main goal of the study is hyperopia correction, we chose patients with little astigmatism (less than 0.50 D) and treated the sphere only. The initial five patients (nine eyes), on average, had 2.50 D of hyperopia and were aged in their 50s; these patients are ideal candidates, as they have mild hyperopia. We over-corrected them up to 0.75 D to help compensate for their presbyopia. Once we confirm that these eyes perform well, the second stage will be to treat eyes with hyperopia and astigmatism.

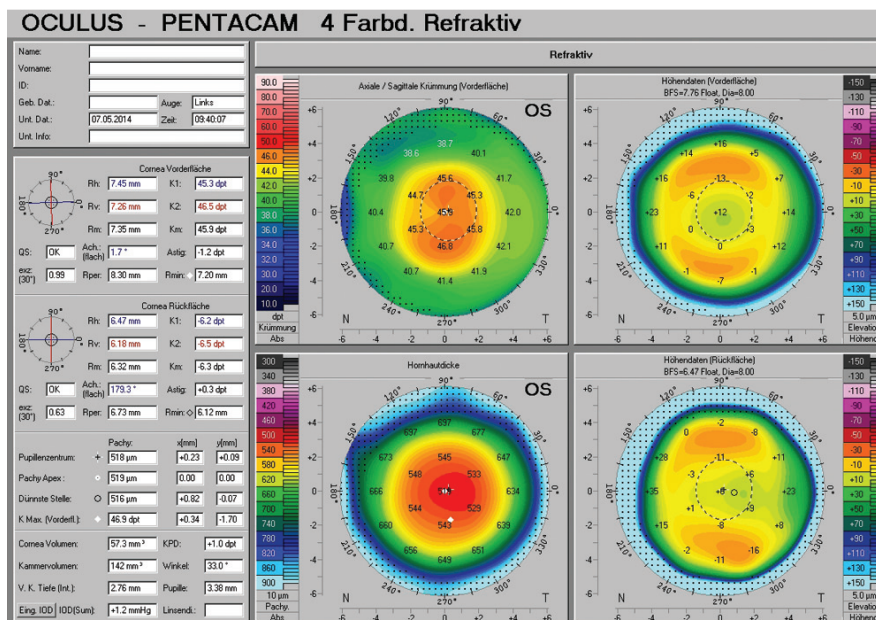
## Question No. 3: What results have you seen thus far?

Because regression can occur up to 6 months after a hyperopic correction, the study will go up to 9 months. At the moment, we have 1-week, 1-month, and 3-month results in all nine eyes, 6-month results in eight eyes, and 9-months results in one eye, and we have not seen any significant regression in the entire cohort (1 week, -0.70 D; 3 months -0.74 D; 6 months, -0.80 D). We are happy because we expect that these results will continue with the other eyes; however, 6-month results do not necessarily reflect the final outcome, so we have to just wait and see. Moreover, we also need time to analyze each individual eye in order to improve our nomograms.

For the time being, we have absolutely stable results and on average no change between 1 week and 3 months. This is unusual for hyperopia correction. It is also important to mention that we did not have any major complications or patient complaints.

## Question No. 4: How do these results show the potential for further development of the flap-free technique that you are using?

Considering the hyperopic treatment, if we show a decent follow-up at 9 months—that we can correct hyperopia with virtually no or little regression—this may mean that we can provide patients with stable, long-term results. Moreover, once the profiles work well, we will switch from ReLEx FLEX to SMILE, achieving other advantages such as a reduced rate of postoperative dry eye that occurs more often after hyperopic laser refractive surgery compared to the myopic treatment.



**Figure 1.** Corneal topography of an eye after a 2.50 D hyperopic ReLEx FLEX treatment. Note the perfect centration of the optical zone.

### Question No. 5: Is SMILE gentler to the corneal architecture than flap-based procedures?

Definitely for the treatment of myopia. Several publications from Turkey and China have shown that the healing response is quicker after SMILE than it is after LASIK and PRK, mainly because fewer nerves are cut and there is less denervation and endothelial cell loss with SMILE than there is with flap-based procedures. This translates to better immediate postoperative comfort and a lower rate of neurotrophic dry eye syndrome than with any other procedure. After 3 to 6 months, there is no difference between procedures in terms of comfort, because the corneal nerves have recovered.

### Question No. 6: Assuming that 9-month results in hyperopic patients are as good as you hope, what is the next step of your study?

Our next two steps would be to: (1) treat patients with hyperopic astigmatism and (2) increase the treatment range.

### Question No. 7: Do you have any closing remarks or take-home messages regarding your recent results?

We are confident that we are on a good path to finding a solution for hyperopia. In the future, I think surgeons will be able to use the VisuMax femtosecond laser (Carl Zeiss Meditec) to treat myopia and myopic astigmatism as well as hyperopia and hyperopic astigmatism. This will change the refractive surgery market, because surgeons can perform a multitude of corrections without an excimer laser. ■

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1. Mohamed-Noriega K, Riau AK, Lwin NC, et al. Early corneal nerve damage and recovery following SMILE (Small Incision Lenticule Extraction) and LASIK (Laser in Situ Keratomileusis). *Invest Ophthalmol Vis Sci*. Published online ahead of print. February 25, 2014. doi:10.1167/iov.13-13324.
2. Mohamed-Noriega K, Riau AK, Lwin NC, et al. Early corneal nerve damage and recovery following small incision lenticule extraction (SMILE) and laser in situ keratomileusis (LASIK). *Invest Ophthalmol Vis Sci*. 2014;55(3):1823-1834.
3. Wei S, Wang Y. Comparison of corneal sensitivity between FS-LASIK and femtosecond lenticule extraction (ReLEx flex) or small-incision lenticule extraction (SMILE) for myopic eyes. *Graefes Arch Clin Exp Ophthalmol*. 2013;251(6):1645-1654. Erratum in: *Graefes Arch Clin Exp Ophthalmol*. 2013;251(10):2495-2497.
4. Ivarsen A, Hjortdal J. New developments in the lenticule extraction procedure. *US Ophthalmol Rev*. 2014;7(1):20-25.
5. Reinsteint DZ, Archer TJ, Randleman JB. Mathematical model to compare the relative tensile strength of the cornea after PRK, LASIK, and small incision lenticule extraction. *J Refract Surg*. 2013;29(7):454-460.
6. Xy Y, Yang U. Dry eye after small incision lenticule extraction and LASIK for myopia. *J Refract Surg*. 2014;30(3):186-190.
7. Roberts C. Biomechanical advantages of SMILE. *Cataract & Refractive Surgery Today Europe*. 2012;9S.
8. Dong Z, Zhou X, Wu J, et al. Small incision lenticule extraction (SMILE) and femtosecond laser LASIK: Comparison of corneal wound healing and inflammation. *Br J Ophthalmol*. doi:10.1136/bjophthalmol-2013-303415.
9. Riau A, Angunawela RI, Charasia SS, et al. Early corneal wound healing and inflammatory response after refractive lenticule extraction (ReLEx). *Invest Ophthalmol Vis Sci*. 2011;52(9):6213-6221.
10. Sekundo W, Gertner J, Bertelmann, Solomatin I. One-year refractive results, contrast sensitivity, high-order aberrations and complications after myopic small-incision lenticule extraction (SMILE). *Graefes Arch Clin Exp Ophthalmol*. 2014;252(5):837-843.
11. Blum M, Kunert KS, Voßmerbäumer U, et al. Femtosecond lenticule extraction (ReLEx) for correction of hyperopia - first results. *Graefes Arch Clin Exp Ophthalmol*. 2013;251(1):349-355.

# Femtosecond Laser Intrastromal Lenticular Implantation

Hyperopic correction goes flapless: One surgeon's approach to minimally invasive hyperopic corrections.

BY SRI GANESH, MBBS, MS, DNB

The treatment of myopia has witnessed tremendous evolution over the past few decades. With the introduction of the VisuMax femtosecond laser (Carl Zeiss Meditec) and the latest all-femtosecond, flapless SMILE solution, it is now possible to correct myopia by creating a refractive lenticule. SMILE, which is emerging as the 3<sup>rd</sup> generation in laser vision correction and a preferred option for treating myopia and myopic astigmatism, is on the verge of replacing LASIK, the current gold standard.

On the other hand, treatment of hyperopia is lagging, with other generations of laser vision correction—LASIK and PRK—being the available and acceptable options. We as refractive surgeons are aware that results of LASIK for hyperopia, especially for higher degrees, are not so gratifying due to issues like regression, induction of aberrations, and high rates of retreatments.<sup>1,2</sup> Some surgeons combine hyperopic LASIK with corneal collagen crosslinking in an attempt to improve biomechanical stability and prevent regression.<sup>3</sup> Independent studies have shown this to be effective in reducing regression; however, the presence of a flap and its weakening effect on corneal biomechanics and the induction of aberrations and postoperative dry eye are issues that need to still be addressed.

## A NEW APPROACH: CRYOPRESERVATION OF CORNEAL LENTICULE

Presently, hyperopia treatment with lenticule extraction is in the clinical trial phase and not yet commercially available. In the meantime, we have found a new application for the VisuMax femtosecond laser, which can be safely and successfully used for hyperopia correction. The technique is called *femtosecond laser intrastromal lenticular implantation* (FILI). Its principle is based on Barraquer's law of tissue addition: If tissue subtraction can correct myopia, then an equal amount of tissue addition should correct hyperopia.<sup>4</sup>

FILI is a new technique that corrects hyperopia by tissue addition rather than tissue subtraction as in LASIK and PRK. It involves insertion of a cryopreserved refractive lenticule, matched for refractive error, into a pocket created in the patient's cornea with the VisuMax femtosecond laser. Experimental research has shown that cryopreservation maintains the morphological details and viability of lenticules extracted after SMILE.<sup>5</sup> Another study in rabbit

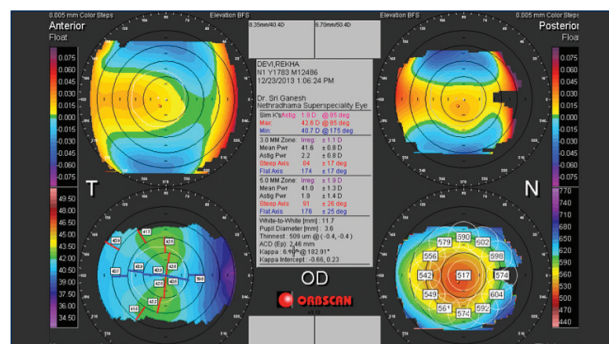


Figure 1. Preoperative topography.

eyes showed it is also possible to restore corneal volume at a later date by reimplanting a lenticule.<sup>6</sup> These results inspired us and also Dr. Kishore and his group<sup>7</sup> to preserve the extracted lenticules and find their suitable application in humans, one of which could be hyperopia correction.

We collected lenticules from healthy patients undergoing myopic correction with SMILE (cap thickness of 100  $\mu$ m, optical zone from 6 to 6.8  $\mu$ m, and a 2-mm superior incision) at our center after obtaining ethics committee approval and the informed consent of the patients as well as testing their serum for transmissible infections. After extraction, lenticules were subjected to a modified tissue technique in a cryobank followed by preservation in liquid nitrogen at  $-192^{\circ}\text{C}$ .

## PROCEDURE

Preoperative planning included detailed anterior and posterior examination, cycloplegic refraction and maximum subjective acceptance, corneal topography with the Orbscan (Bausch + Lomb) and Cirrus OCT (Carl Zeiss Meditec), specular microscopy, and dry eye assessment. The cryopreserved lenticule, matched with the hyperopic error of the patient undergoing FILI, was thawed manually and washed in balanced saline solution to remove the cryoprotectant agents before implantation.

Using the VisuMax femtosecond laser, a pocket was created in the cornea at a depth of 160  $\mu$ m and a diameter varying from 7 to 7.8  $\mu$ m, depending on the optical zone of the cryopreserved tissue. The lenticule was marked in center and inserted into the patient's cornea through a 4-mm superior incision. After insertion, the



TABLE 1. EXAMPLE OF PRE- AND POSTOPERATIVE DATA

Patient/Eye	BCVA	Spherical equivalent (D)	Mean keratometry (D)	Central thickness ( $\mu\text{m}$ )	Q value	Endothelial cell density (cells/ $\text{mm}^2$ )	Schirmer test (mm)
Preoperative	6/18	6.50	41.60	519	-0.39	2,892	> 25
6-month postoperative	6/12	0.50	45.50	581	-0.83	2,883	> 25

center of the lenticule was spread out and aligned with the patient's pupillary center. Postoperatively, topical steroids were prescribed in tapering dosage for 3 months.

Our initial experience with six eyes has shown the procedure to be safe, with good refractive predictability. There was no rejection or adverse reactions by the end of 6 months.

### CASE PRESENTATION

A 32-year-old woman underwent FILI in her right eye for 6.50 D of hyperopia (Figure 1). Her preoperative and 6-month postoperative data is summarized in Table 1. A clear and well-centered lenticule was visible at 6 months postoperatively (Figures 2 and 3). Note the normal epithelial thickness profile on anterior segment optical coherence tomography (AS-OCT). On topography, 1.00 D of against-the-rule astigmatism is seen (Figure 4), due to the superior 4-mm incision; however, it settled over time.

It is interesting to note that the postoperative Q value for the 6.50 D correction was -0.83, suggesting slight change toward a hyperprolate shape, unlike hyperopic LASIK which makes the cornea highly hyperprolate. With this treatment, typical Q values exceed -1.5 to -2 for the same degree of correction. This change in corneal shape to abnormal hyperprolate is due to the ablation of mid-peripheral tissue, which is the main cause for regression and higher-order aberrations after hyperopic LASIK. FILI nearly maintains the natural shape of cornea, thus minimizing chances of regression. Faster healing and visual recovery, the avoidance of flap-related com-

plications, fewer dry eye symptoms, minimal chance of rejection, and reversibility are also potential advantages of this procedure.

### CONCLUSION

It is too early to say that FILI can replace LASIK for hyperopia treatment, as longer follow-up and modification in surgical technique to reduce induced astigmatism are required and nomograms must be developed to achieve the most accurate results. Nevertheless, the novelty of this flapless procedure and its potential advantages may prompt further research before it is accepted as a valid treatment option for hyperopia. ■

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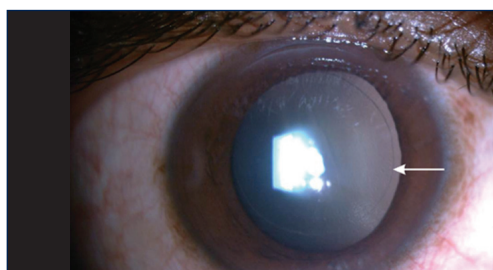


Figure 2. Six-month postoperative clinical picture showing the edge of lenticule (arrow) on retroillumination.

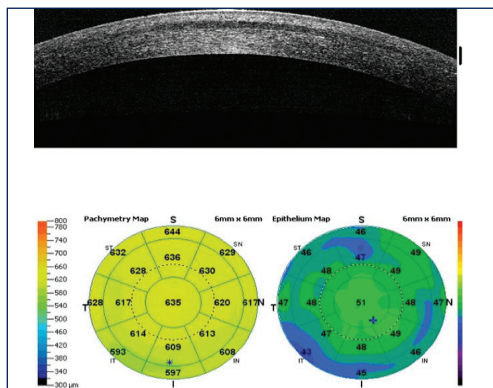


Figure 3. Six-month postoperative anterior segment OCT (top) showing a well-centered lenticule with a clear interface and normal epithelial thickness profile. Pachymetry (bottom left) and epithelial (bottom right) maps.

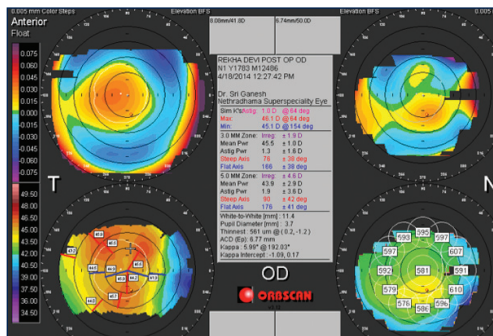


Figure 4. Six-month postoperative topography.

1. Jaycock PD, O'Brart DP, Rajan MS, Marshall J. 5-year follow up of LASIK for hyperopia. *Ophthalmology*. 2005;112(2):191-199.
2. Llorente L, Barbero S, Merayo J, Marcos J. Total and corneal aberrations by laser in situ keratomileusis for hyperopia. *J Refract Surg*. 2004;20(3):203-216.
3. Kanellopoulos AJ, Kahn J. Topography-guided hyperopic LASIK with and without high irradiance collagen cross-linking: Initial comparative clinical findings in a contralateral eye study of 34 consecutive patients. *J Refract Surg*. 2012;28:S837-S840.
4. Barraquer JI. Refractive corneal surgery. Experience and considerations. *An Inst Barraquer*. 1993;94:24:113-118.
5. Mohamed-Noriega K, Toh KP, Poh R. Cornea lenticule viability and structural integrity after refractive lenticule extraction (ReLEx) and cryopreservation. *Molecular Vision*. 2011;17:3437-3449.
6. Angunawela RJ, Riau AK, Chaurasia SS. Refractive lenticule re-implantation after myopic ReLEx: A feasibility study of stromal restoration after refractive surgery in a rabbit model. *Invest Ophthalmol Vis Sci*. 2012;53:4975-4985.
7. Pradhan KR, Reinstein DZ, Carp GL, et al. Femtosecond laser-assisted keyhole endokeratophakia: correction of hyperopia by implantation of an allogeneic lenticule obtained by SMILE from a myopic donor. *J Refract Surg*. 2013;29(11):777-782.